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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/608,516	06/26/2003	Mark A. Kay	STAN-160CIPCON	9310

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EXAMINER	
CROUCH, DEBORAH	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/608,516	KAY ET AL.	
	Examiner	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/30/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 1-30 are pending.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-30 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-33 of U.S. Patent No. 6.613,752. Although the conflicting claims are not identical, they are not patentably distinct from each other because present claims 1-30 are generic to claims 1-33 of '752.

Present claims 1-30 are drawn to a method of integrating an exogenous nucleic acid into the genome of at least one cell of multicellular organism, a method of inserting an exogenous nucleic acid into the genome of a at least one cell of a mammal, a method for expressing an exogenous gene in at least one cell of a multicellular organism, a method for enhancing the amount of a protein present in a multicellular organism and a method of in vivo gene transfer of a gene into the genome of at least one cell of a multicellular organism each comprising administering to a multicellular organism or mammal a Sleeping Beauty transposon and a source of Sleeping Beauty transposase.

Claims 1-33 of '752 are drawn to a method of integrating an exogenous nucleic acid into the genome of at least one hepatic cell of a multicellular organism, a method of inserting an exogenous nucleic acid into the genome of at least one hepatic cell of a mammal, a method for expressing an exogenous gene in at least one hepatic cell of a multicellular organism, a method for expressing in a multicellular organism, and a method of in vivo gene transfer of a gene into the genome of at least one cell of a multicellular organism comprising administering directly to said multicellular organism a Sleeping Beauty Transposon comprising said gene flanked by a first inverted repeat have a sequence of SEQ ID NO: 18 and a second inverted repeat sequence having a sequence of SEQ ID NO: 19 and a source of Sleeping Beauty transposase that has a sequence of SEQ ID NO: 01.

The present claims anticipate, and are generic to claims 1-33 of '752. The present specification defines each term of the present claims to encompass the terms of claims 1-33 of '752. Thus at the time of filing the skilled artisan would have reached the present claims given claims 1-33 of '752.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of integrating an exogenous nucleic acid into the genome of at least one cell of mammal, a method of inserting an exogenous nucleic acid into the genome of a at least one cell of a mammal, a method for expressing an exogenous gene in at least one cell of a mammal, a method for enhancing the amount of a protein present in a mammal and a method of in vivo gene transfer of a gene into the genome of at least one cell of a mammal each comprising administering directly to a target

tissue of a mammal a Sleeping Beauty Transposon comprising said gene flanked by a first inverted repeat and a second inverted repeat sequence and a nucleic acid encoding Sleeping Beauty transposase, does not reasonably provide enablement for the claimed methods of delivery to the genus of multicellular organisms, the gene of interest not having Sleeping Beauty transposon invert repeats flanking the gene, and the transposase delivered by other than a nucleic acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are only enabled for delivery to mammals. The specification discloses the Sleep Beauty transposon system to be useful for to characterize a particular gene, where the transposon system inserts a gene of interest into a target cell and the effect of the insertion is observed in the target cell. However, this particular method is not seen as within the scope of the claims as the claims are to methods involving multicellular organisms. The insertion mutagenesis implementation of the Sleeping Beauty transposon is not disclosed for whole organism mutagenesis, but for "target cells." This application is viewed as cells in culture or otherwise isolated cells. Polypeptide synthesis and therapeutic applications are disclosed to be applied to "multicellular organisms," but there is no evidence that Sleeping Beauty transposons will cause the insertion into the genome of organisms other than mammals. Applicant's disclosure of mice treated with the Sleeping Beauty transposons of the invention indicates that the system will function in all mammals sufficiently to make recoverable quantities of protein or to provide a therapeutic effect. For both of these uses, recoverable quantities of protein or therapeutic effects have only been shown in mammals, as exemplified by mammals. While the art teaches multiple vertebrate cell lines that have been transformed by Sleeping Beauty, the in vivo nature of the claims makes the degree of transformation critical. Cells in culture cannot reasonably be expected to mimic the in vivo

situation, as the route of delivery would be critical for the successful transformation of target tissues to have a therapeutic effect. It is also notice that in each instance of a successful therapeutic effect using the Sleeping Beauty transposon system, the transposon and DNA sequence encoding the transposase, was directly administered to the relevant tissue in mice models of various human disease.

Thus at the time of the present invention, it would have taken an undue amount of experimentation without a predictable degree of success to implement the claimed invention for its entire breadth.

Claims 1-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

The only Sleeping Beauty Transposon inverted repeats described are a first inverted repeat having a sequence of SEQ ID NO: 18 and a second inverted repeat sequence having a sequence of SEQ ID NO: 19. The only Sleeping Beauty transposase described has a sequence of SEQ ID NO: 01. There is no evidence that applicant had conceived of or was in possession of inverted repeats and transposases other than those specifically disclosed.

Therefore, description of SEQ ID NO:18, SEQ ID NO: 19 and SEQ ID NO: 01 fails to fulfill the written description requirement for the claimed genus because one could not have envisioned the primary structure of other nucleotides encoding the inverted repeats of the Sleeping Beauty transposon, or other amino acid sequences encoding the Sleeping Beauty transposase. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641,1646 (1998). There are no detailed drawings or relevant descriptions for the breath of the claims to indicate possession of the claimed invention to the skilled artisan at the time of filing.

With the exception of the sequence referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, and therefore conception is not achieved until reduction to practice has occurred regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Futher, transposases recognize very specifically the target sequence. The Sleeping Beauty transposase of SEQ ID NO: 1 would not be expected to recognize inverted repeats other than those of SEQ ID NO: 18 and 19. Likewise, SEQ ID NO: 18 and 19 are unlikely to

be recognized by transposases with an amino acid sequence different from SEQ ID NO: 1. Applicant has not provided description of any such inverted repeats or transposases that will function in the Sleeping Beauty transposon system. Without such description, applicant would not be considered to be in possession of the claimed invention for its breath by the skilled artisan at the time of filing.

In view of the above considerations one of skill in the art would not recognize that applicant was in possession of the necessary common features or attributes possessed by any member of the genus of Sleeping Beauty transposon or Sleep Beauty transposase other than that set forth by SEQ ID NO:18, 19 and 1. Therefore, only the Sleeping Beauty transposon invert repeats and Sleeping Beauty transposase which meet written description are, thus, those depicted in SEQ ID NO: 18, 19 and 1. University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that "to fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention".

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The claims are free of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 571-272-0727. The examiner can normally be reached on M-Fri, 7:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deborah Crouch

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

December 23, 2005